UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,914	08/10/2001	Timothy P. Tully	17VV-137270	5180

68850 7590 04/27/2010

DON J. PELTO
Sheppard, Mullin, Richter & Hampton LLP
1300 I STREET, NW
11TH FLOOR EAST
WASHINGTON, DC 20005

EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
04/27/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/927,914	TULLY ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10,12,13,21,22,24-48,59,65-93,100-104,107 and 108* is/are pending in the application.

4a) Of the above claim(s) *2,9,10,12,13,21,22,24-48,59 and 65-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-8, 100-104, 107-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 1/28/10. Claim(s) 3, 11, 14-20, 23, 49-58, 60-64, 94-99, 105-106 have been cancelled. Claim(s) 107-108 have been added. Claim(s) 1-2, 4-10, 12-13, 21-22, 24-48, 59, 65-93, 100-104, 107-108 are pending. Claim(s) 1, 100-102, 104 have been amended. Claim(s) 2, 9-10, 12-13, 21-22, 24-48, 59, 65-93 have been withdrawn. Claim(s) 1, 4-8, 100-104, 107-108 are examined herein.

Applicant's amendments to the claims have rendered all 112 rejections of the last Office Action moot, therefore hereby withdrawn.

Applicant's arguments with regard to the 103(a) rejection of the last Office Action have been fully considered but found not persuasive. The 103(a) rejection of the last Office Action is maintained for reasons of record and modified below as a result of Applicant's amendments to the claims.

The following new rejections will also apply.

Claim Objections

Claim 4 is objected to because of the following informalities: Claim 4 should recite "step (a)" instead of "step b)". Appropriate correction is required.

Claims 100-104 are objected to because of the following informalities: Claims 100-104 are identical to claims 4-8. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 5 and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, dependent claims 5 and 101 recites the limitation “wherein said phosphodiesterase 4 inhibitor is administered before and during each training session” which is a broader recitation than the limitation in claim 1 which recites “administering a phosphodiesterase 4 inhibitor to said animal during rehabilitation.”

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-8, 100-104, 107-108 are rejected under 35 U.S.C. 103(a) as being obvious over Christensen et al. (US Patent 5,547,979) in view of the Merck Manual (of record).

The instant claims are directed to a method of providing cognitive training and administering a phosphodiesterase 4 inhibitor to a human during rehabilitation of said animal from stroke, wherein the human has suffered impaired cognitive function and impaired sensory-motor function due to the stroke.

Christensen et al. teach the phosphodiesterase inhibitor, rolipram (col. 11, line 14), in a method of treating stroke in a human (claim 1). The active ingredient may be administered from 1 to 6 times a day (col. 8, lines 62-64) or as recognized by one of

ordinary skill in the art that the optimal quantity and spacing of individual dosages will be determined by the nature and extent of the condition, the form, route, site of administration, patient, and that such optimums can be determined by conventional techniques (col. 10, lines 29-41).

It is noted that the limitations regarding "which enhances CREB pathway function" and "wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain" are given little patentable weight, because these biological processes are inherent when the same compound is administered in the same patient population at the same dosage.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Examiner also notes that one of ordinary skill in the art would recognize that stroke patients are usually characterized by impaired cognitive function as well as impaired sensory-motor function. Moreover, the giving multiple cognitive training sessions to a stroke patient is necessitated by a clinical diagnosis of one or both of impaired cognitive function and impaired sensory-motor function.

However, Christensen et al. fail to disclose multiple cognitive training sessions sufficient to produce an improvement in performance of a cognitive task whose deficit is associated with a central nervous system disorder to an animal during rehabilitation of said animal from stroke.

The Merck Manual teaches that a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises, if possible, should be started early (pg. 1455-1456). It is noted that these rehabilitation techniques meet the limitation of cognitive training. Furthermore, it is obvious to one of ordinary skill in the art to not stop at a single training session in the rehabilitation of a stroke victim since the process takes a great deal of time with many repeated sessions.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of treating stroke in a human, as disclosed by Christensen et al. during rehabilitation of said human from stroke.

A person of ordinary skill in the art would have been motivated to combine the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of

treating stroke in a human, as disclosed by Christensen et al. during rehabilitation of said human from stroke because: (1) both Christensen and the Merck Manual disclose treatment for the same purpose, which is treating stroke patients and because (2) of the additive therapeutic effects of employing two methods of treating stroke simultaneously. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating stroke in a human by administering a phosphodiesterase inhibitor, rolipram, in conjunction with a cognitive training protocol, outlined by the Merck Manual during rehabilitation of said human from stroke.

Response to Arguments

Applicant argues that no evidentiary basis for the assertion that Christensen covers PDE4 inhibitor administration during all stages of stroke treatment has been made. Christensen does not expressly or inherently disclose administering a PDE4 inhibitor during rehabilitation of a stroke patient. Specifically, Applicants go into great detail regarding the mechanism of action of PDE4 inhibitors, including inhibiting the inflammatory response often associated during the immediate time period following a brain injury. Therefore, Christensen effectively teaches away from the repeated application of PDE4 inhibitors in conjunction with stroke, due to the early production of TNF during the initial stages of an inflammatory event.

This is not persuasive because Christensen clearly does not limit the administration of PDE4 inhibitors to any particular time period or treatment window of a stroke patient. In fact, Christensen clearly recites the treatment of a stroke patient,

which also includes the time after the acute phase of stroke episode or the rehabilitation period involving cognitive training. One of ordinary skill in the art would interpret the teachings of Christensen to administer the PDE4 inhibitor after the acute phase of stroke episode since a full clinical diagnosis must be made before any treatment regimen is to be implemented. The skilled artisan would also recognize that rehabilitation should be started as soon as a full diagnosis is made. Further, it is not clear when exactly does inflammation subside during the treatment period of a stroke patient, since low levels of inflammation could last well into the rehabilitation period. Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Applicant continues to argue that Christensen does not mention rehabilitation and only mentions stroke twice.

This is not persuasive because if Christensen were to mention rehabilitation, then the rejection would be anticipatory. Applicant is reminded that the current rejection is a 103(a) rejection based on obviousness, where the Merck Manual teachings rehabilitation of stroke patients. Further, the fact that stroke is only mentioned twice does not take anything away from the teachings of Christensen since the reference teaches the exact patient population as claimed.

Applicant also argues that the Merck Manual can only be read to teach cognitive training after the acute phase of a stroke. As a result, Applicant argues against the motivation in the obviousness rejection.

This is not persuasive because as stated above, Christensen clearly teaches, in general, the treatment of a stroke patient by administering a PDE4 inhibitor, which encompasses the entire treatment regimen including rehabilitation. Furthermore, the Merck Manual clearly state that a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises, if possible, should be started early. This time period may encompass when the patient is still in or just recovering from the acute phase of the stroke episode and beyond. Nonetheless, it is clear that the Merck Manual teaches cognitive training after the acute phase of a stroke. It is Examiner's position that it would be obvious to administer PDE4 inhibitors as taught by Christensen in combination with rehabilitation after the acute phase of stroke. Therefore, since both references teach treating stoke patients, it is obvious to combine these treatment regimens because both are drawn to the same purpose as well as for the combined therapeutic effect. For these reasons, Examiner submits that there would be reasonable expectation of success in treating stroke patients as instantly claimed. Applicant's arguments directed to two different treatments, whose roles in stroke are mechanistically, temporally, and clinically distinct, are not persuasive. The reason being that although the mechanism of action may be different, the ultimate goal of treating stroke is the same. It is Examiner's position that both treatment regimens serve to work together in treating a stroke patient through rehabilitation.

Applicant argues hindsight reconstruction in the argument that performance gain would necessarily result if rolipram therapy is administered immediately following stoke and cognitive therapy is begun as early as possible after stroke. Applicant argues that the Examiner has provided no evidence that the administration timeline contemplated by Christensen overlaps with that described by the Merck Manual. Specifically, Applicant argues that neither of the cited references teach or suggest "long-lasting performance gain effected by enhancement of CREB pathway function during rehabilitation."

This is not persuasive because said performance gain of a cognitive task in a stroke patient is an inherent property when the same compound is administered to the same patient at the same dose. Therefore, the "long lasting" and "enhancement of CREB pathway function" limitations are met because they are inherent properties. Moreover, the Examiner interprets performance gain of a cognitive task as covering a wide range of impairments, which include aphasia (language/speech disturbance) and apraxia (impaired ability to carry out motor activities), as disclosed in Applicant's own disclosure. Essentially, the scope of the instant claims covers administration of the phosphodiesterase inhibitors at any time to the patient. Therefore, Applicant's assertion that Christensen is simply teaching the administration of rolipram during the acute phase of the stroke to reduce TNF still meets the limitations of the instant claims as it relates to the Merck Manual reference. Nonetheless, Applicant is invited to show factual data that performance gain would not result in the method taught by the cited prior art references.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/
Primary Examiner, Art Unit 1627

YSC